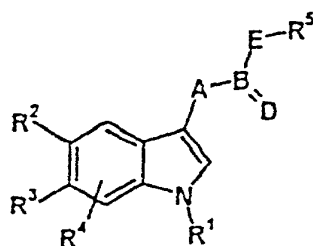


We claim:

1. A compound of the Formula



(1)

and their pharmaceutically acceptable salts, wherein

R^1 , R^5 are independently of each other

(i) a C_{1-2} alkyl, straight-chain or branched-chain, optionally mono- or polysubstituted by -OH, -SH, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl, -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl), -NHCOR⁶, -NO₂, -CN, -F, -Cl, -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -O(CO)R⁶, -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶, -SO₃H, -SO₂R⁶, -OSO₂C₁₋₆ alkyl, -OSO₂C₆₋₁₄ aryl, -(CS)R⁶, -COOH, -(CO)R⁶, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C₆₋₁₄ aryl groups and the included carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R⁴,

(ii) -C₂₋₁₂ alkenyl, mono- or polyunsaturated, straight-chain or branched-chain, optionally mono- or polysubstituted by -OH, -SH, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl, -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl), -NHCOR⁶, -NO₂, -CN, -F, -Cl, -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -O(CO)R⁶, -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶, -SO₃H, -SO₂R⁶, -OSO₂C₁₋₆ alkyl, -OSO₂C₆₋₁₄ aryl, -(CS)R⁶, -COOH, -(CO)R⁶, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or

23 tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to
24 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and
25 S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic
26 substituents for their part can optionally be mono- or polysubstituted by R^4 ,

27 (iii) mono-, bi- or tricyclic saturated or mono- or polyunsaturated
28 carbocycles having from 3 to 14 ring members, optionally mono- or
29 polysubstituted by -OH, -SH, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄
30 aryl, -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl), -NHCOR⁶, -NO₂, -CN, -F, -Cl,
31 -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -O(CO)R⁶, -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶,
32 -SO₃H, -SO₂R⁶, -OSO₂C₁₋₆ alkyl, -OSO₂C₆₋₁₄ aryl, -(CS)R⁶, -COOH, -(CO)R⁶,
33 mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles
34 having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono-
35 or polyunsaturated heterocycles having from 5 to 15 ring members and from 1
36 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups
37 and the included carbocyclic and heterocyclic substituents can optionally be
38 mono- or polysubstituted by R^4 ,

39 (iv) mono-, bi- or tricyclic saturated or mono- or polyunsaturated
40 heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms,
41 which are suitably N, O and S, optionally mono- or polysubstituted by -OH,
42 -SH, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl, -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆
43 alkyl)(C₆₋₁₄ aryl), -NHCOR⁶, -NO₂, -CN, -F, -Cl, -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄
44 aryl, -O(CO)R⁶, -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶, -SO₃H, -SO₂R⁶, -OSO₂C₁₋₆
45 alkyl, -OSO₂C₆₋₁₄ aryl, -(CS)R⁶, -COOH, -(CO)R⁶, mono-, bi- or tricyclic
46 saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring
47 members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated
48 heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms,
49 which are suitably N, O and S, where the C_{6-14} aryl groups and the included
50 carbocyclic and heterocyclic substituents for their part can be optionally
51 mono- or polysubstituted by R^4 , -carbo- or heterocyclic saturated or mono- or

52 polyunsaturated spirocycles having from 3 to 10 ring members, where
 53 heterocyclic systems contains from 1 to 6 heteroatoms, which are suitably N,
 54 O and S, optionally mono- or polysubstituted by -OH, -SH, -NH₂, -NHC₁₋₆
 55 alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl, -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl),
 56 -NHCOR⁶, -NO₂, -CN, -F, -Cl, -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -O(CO)R⁶,
 57 -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶, -SO₃H, -SO₂R⁶, -OSO₂C₁₋₆ alkyl, -OSO₂C₆₋₁₄
 58 aryl, -(CS)R⁶, -COOH, -(CO)R⁶, mono-, bi- or tricyclic saturated or mono- or
 59 polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or
 60 tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to
 61 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and
 62 S, where the C₆₋₁₄ aryl groups and the included carbocyclic and heterocyclic
 63 substituents can optionally be mono- or polysubstituted by R⁴,
 64 R², R³ are hydrogen or -OH, where at least one of the two substituents must
 65 be -OH;
 66 R⁴ is -H, -OH, -SH, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl,
 67 -N(C₆₋₁₄ aryl)₂, -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl), -NHCOR⁶, -NO₂, -CN, -COOH,
 68 -(CO)R⁶, -(CS)R⁶, -F, -Cl, -Br, -I, -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -O(CO)R⁶,
 69 -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl, -SOR⁶, -SO₂R⁶.
 70 R⁶ is -H, -NH₂, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NHC₆₋₁₄ aryl, -N(C₆₋₁₄ aryl)₂,
 71 -N(C₁₋₆ alkyl)(C₆₋₁₄ aryl), -O-C₁₋₆ alkyl, -O-C₆₋₁₄ aryl, -S-C₁₋₆ alkyl, -S-C₆₋₁₄ aryl,
 72 -C₁₋₁₂ alkyl, straight-chain or branched-chain, -C₂₋₁₂ alkenyl, mono- or
 73 polyunsaturated, straight-chain or branched-chain, -mono-, bi- or tricyclic
 74 saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring
 75 members, -mono-, bi- or tricyclic saturated or mono- or polyunsaturated
 76 heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms,
 77 which are suitably N, O and S;
 78 A is either a bond, or -(CH₂)_m-, -(CH₂)_m-(CH=CH)_n-(CH₂)_p-, -(CHOZ)_m-,
 79 -(C=O)-, -(C=S)-, -(C=N-Z)-, -O-, -S-, -NZ-, where m and p are cardinal
 80 numbers from 0 to 3 and n is a cardinal number from 0 to 2,

81 Z is H, or a C_{1-12} alkyl, straight-chain or branched-chain, C_{2-12} alkenyl,
82 mono- or polyunsaturated, straight-chain or branched-chain, mono-, bi- or
83 tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to
84 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyun-
85 saturated heterocycles having from 5 to 15 ring members and from 1 to 6
86 heteroatoms, which are suitably N, O and S;
87 B is either carbon or sulfur, or $-(S=O)-$;
88 D is oxygen, sulfur, CH_2 or N-Z, where D can only be S or CH_2 if B is
89 carbon;
90 E is a bond, or $(CH_2)_m$, $-O-$, $-S-$, $-(N-Z)-$, where m and Z have the same
91 meanings as above.

1 2. The compound of claim 1, wherein the compound is a pharma-
2 ceutically acceptable salt of an organic or inorganic acid, or of an organic or
3 inorganic base, or a quaternary ammonium salt from the quaternization of a
4 tertiary amine.

1 3. The compound of claim 1, having an asymmetric carbon atom by
2 being the L or the D form, or a D,L mixture, and when in a
3 diastereoisomeric form.

1 4. A compound of claim 1, being one of the following compounds:

2 N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-
3 oxoacetamide;

4 N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-
5 oxoacetamide Na salt;

6 N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-
7 hydroxyacetamide;

8 N-(pyridin-4-yl)-2-[1-(2,6-difluorobenzyl)-5-hydroxyindol-3-yl]-2-
 9 oxyacetamide;
 10 N-(3,5-dichloropyridin-4-yl)-2-[1-(2,6-difluorobenzyl)-5-hydroxyindol-3-
 11 yl]-2-oxoacetamide;
 12 N-(3,5-dichloropyridin-4-yl)-2-[1-(3-nitrobenzyl)-5-hydroxyindol-3-yl]-2-
 13 oxoacetamide Na salt;
 14 N-(3,5-dichloropyridin-4-yl)-2-(1-propyl-5-hydroxyindol-3-yl)-2-
 15 oxyacetamide;
 16 N-(3,5-dichloropyridin-4-yl)-2-(1-isopropyl-5-hydroxyindol-3-yl)-2-
 17 oxoacetamide;
 18 N-(3,5-dichloropyridin-4-yl)-2-(1-cyclopentylmethyl-5-hydroxyindol-3-yl)-
 19 2-oxoacetamide;
 20 N-(2,6-dichlorophenyl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-
 21 oxoacetamide;
 22 N-(2,6-dichloro-4-trifluoromethylphenyl)-2-[1-(4-fluorobenzyl)-5-
 23 hydroxyindol-3-yl]-2-oxoacetamide;
 24 N-(2,6-dichloro-4-trifluoromethoxyphenyl)-2-[1-(4-fluorobenzyl)-5-
 25 hydroxyindol-3-yl]-2-oxoacetamide;
 26 N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-6-hydroxyindol-3-yl]-2-
 27 oxoacetamide;
 28 N-(3,5-dichloropyridin-4-yl)-5-hydroxy-1-(4-methoxybenzyl)indole-3-
 29 carboxamide.

1 5. A process for preparing compounds of claim 1, which comprises
 2 converting a compound of claim 1 wherein R₁ or R³, or R² and R³ is -O-R⁷ in
 3 which R⁷ is a leaving group.

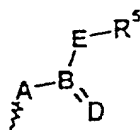
1 6. The process of claim 5, wherein said leaving group is alkyl,
 2 cycloalkyl, arylalkyl, aryl, heteroaryl, acyl, alkoxycarbonyl, aryloxy carbonyl,

3 aminocarbonyl, N-substituted aminocarbonyl, silyl or sulfonyl residue or a
4 complexing agent.

1 7. The process of claim 6, wherein said complexing agent is a
2 compound of boric acid or phosphoric acid, or a compound containing a
3 covalently bonded metal.

1 8. The process of claim 7, wherein said metal is zinc, aluminum,
2 or copper.

1 9. A process for preparing compounds of claim 1, which comprises
2 converting the substructure



3
4 into another compound of claim 1.

1 10. A process for inhibiting $\text{TNF}\alpha$ by administering to a patient in
2 need therefor an effective amount of the compound of claim 1.

1 11. A process for inhibiting $\text{TNF}\alpha$ by administering to a patient in
2 need therefor an effective amount of the compound of claim 4.

1 12. A process for inhibiting phosphodiesterase 4 by administering
2 to a patient in need therefor an effective amount of the compound of claim
3 1.

1 13. A process for inhibiting phosphodiesterase 4 by administering
2 to a patient in need therefor an effective amount of the compound of claim
3 4.

1 14. A process for treating an eosinophil-related condition by
2 administering to a patient in need therefor an effective amount of the
3 compound of claim 1.

1 15. A process for treating an eosinophil-related condition by
2 administering to a patient in need therefor an effective amount of the
3 compound of claim 4.

1 16. A process for treating a chronic obstructive pulmonary disease,
2 which comprises administering to a patient in need therefor an effective
3 amount of a compound of claim 1.

1 17. A process for treating a chronic obstructive pulmonary disease,
2 which comprises administering to a patient in need therefor an effective
3 amount of a compound of claim 4.

1 18. A process for treating arthritis, rheumatoid arthritis,
2 spondylitis, osteoarthritis, sepsis, septic shock, gram negative sepsis, toxic
3 shock syndrome, respiratory distress syndrome, asthma, chronic pulmonary
4 disorders, bone resorption diseases, transplant rejection reactions, autoimmune
5 disorders, lupus erythematosus, multiple sclerosis, glomerulonephritis, uveitis,
6 insulin dependent diabetes mellitus, chronic demyelination, malaria,
7 infection-related fever, infection-related myalgia, AIDS, cachexia, bronchial
8 asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, eczema,
9 allergic angitis, eosinophilic fasciitis, eosinophilic pneumonia, pulmonary

10 infiltration with eosinophilia, urticaria, ulcerative colitis, Crohn's disease,
11 psoriasis, keratosis, pulmonary neutrophilic infiltration, chronic obstructive
12 pulmonary disease, senile dementia, loss of memory, Parkinson's disease,
13 depression, stroke, intermittent claudication, benign prostate hyperplasia,
14 pollakuria, nycturia, bladder atony, kidney stone colics, and analgesic
15 dependency, which comprises administering to a patient a pharmacologically
16 effective amount of a compound of claim 1.

1 19. A pharmaceutical preparation which comprises a
2 therapeutically effective amount of the compound of claim 1, together with
3 one or more of a pharmaceutically acceptable carrier, diluent, and auxiliary
4 ingredient.

1 20. A process for preparing the pharmaceutical preparation of
2 claim 12, which comprises preparing a pharmaceutically acceptable dosage
3 form from a compound of claim 1, and from one or more of a pharma-
4 ceutically acceptable carrier, diluent, and auxiliary ingredient.